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A case of lethal congenital dwarfism with accelerated skeletal maturation

S. Blomstrand[1], I. Claëson[2] and J. Säve-Söderbergh[3]

Departments of [1]Pediatrics and [2]Radiology, Childrens Hospital, Östra Sjukhuset, and [3]Department of Pathology, Östra Sjukhuset, University of Göteborg, Göteborg, Sweden

Abstract. Details of a female infant, who was born after 29 weeks gestation and who died within minutes of birth, are presented. The infant was hydropic, showed macroglossia and had very short limbs with normal sized hands and feet. Apart from a preductal aortic coarctation the pathological findings were confined to the skeleton. The radiographical and histological findings are described in detail; they differ from those of previous studies of similar conditions.

Case report

The infant was a first child of a 22-year-old woman, who 6 years earlier had a spontaneous second trimester abortion. The child's parents were Finnish and were closely related, both having the same father. No earlier cases of dwarfism, stillbirths on neonatal deaths were known in the family. Hydramniosis was suspected in the 28th week of pregnancy. Ultrasound examination confirmed this and showed a hydropic fetus. Amniocentesis showed normal α-fetoprotein (4 mg/l) and normal female chromosomes. No isoimmunization was found in the mother. One week later labour started and an immature female infant was born. The Apgar score at 1 min was 1 due to irregular heartbeats, which soon ceased.

The infant was short (0.28 m), and weighed 1.41 kg. She had very short limbs with almost normal hands and feet. There was a general oedema and a large swollen tongue, which had probably prevented swallowing and also blocked the airway (Fig. 1A).

Radiographs of the skeleton showed the following characteristics (Fig. 1B–F): *Skull* – a comparatively small facial skeleton to the cranial vault. The base of the skull was short, the nasal bridge depressed and the mandible hypoplastic. The hyoid bone was well mineralized, as were the laryngeal cartilage. *Thorax and spine* – the thorax was long and narrow with a uniform widening of the anterior ends of the short horizontal ribs. The vertebral bodies had a normal appearance with normal interpedicular and intervertebral spaces. The sacral and coccygeal vertebrae were ossified. In the pelvis the iliac bones were squared and the ischial and pubic bones were of normal size and shape. *Limbs* – the long tubular bones were extremely short, were not bowed, and had marked metaphyseal flaring and cupping. The ossified femora were only 22 mm long. The metacarpal and carpal bones as well as the tarsal and metatarsal bones were wide and short. Markedly advanced ossification of carpal and tarsal bones was present and four tarsal bones on each side could easily be identified.

The autopsy showed a preductal aortic coarctation as the only malformation of the internal organs. The weights of the heart, thymus, spleen and kidneys were below those considered normal for a fetal weight of between 1.0 and 1.5 kg, while the liver, brain, thyroid and adrenal glands were of normal weight. All these organs were of normal histologic structure. The decalcified 5 µm sections that were taken from the larynx and different bones were all abnormal.

The larynx showed ossification of the cartilages, with only a small amount of cartilage in the periphery (Fig. 2A). The appearance was that of a spongy bone with red bone marrow, the individual bone trabeculae being irregular and coarse. The hyoid bone was also ossified. Normal membraneous ossification was present in the parietal bones. The cartilagenous ossification in the other bones was also abnormal with a reduced amount of cartilage and an abnormal bone structure. The malformed long bones were studied in the region of the knee (Fig. 2B). The femur had a bent shaft with a club-shaped distal end. The epiphysis consisted only of a thin cap of cartilage and no secondary ossification centres could be found. The epiphyseal-metaphyseal junction was reduced in height and was of irregular form (Fig. 2B). The zones of resting and proliferating cartilage were thin and irregular, and the zone of transformation was also thin and unevenly developed. In the zone of ossification the bone trabeculae were thin and haphazardly oriented, and red bone marrow could be seen between them. In the shafts of the long bones the structure was more compact with coarse bone trabeculae leaving little room for a hypocellular marrow. The bone structure was partly lamellar and partly woven.

Discussion

Achondrogenesis and thanatophoric dwarfism are the best known forms of congenital dwarfism leading to neonatal death. In both conditions the limbs are extremely short as in our case [1]. Achondrogenesis in particular has been described in association with a femur length of less than 30 mm. However, the

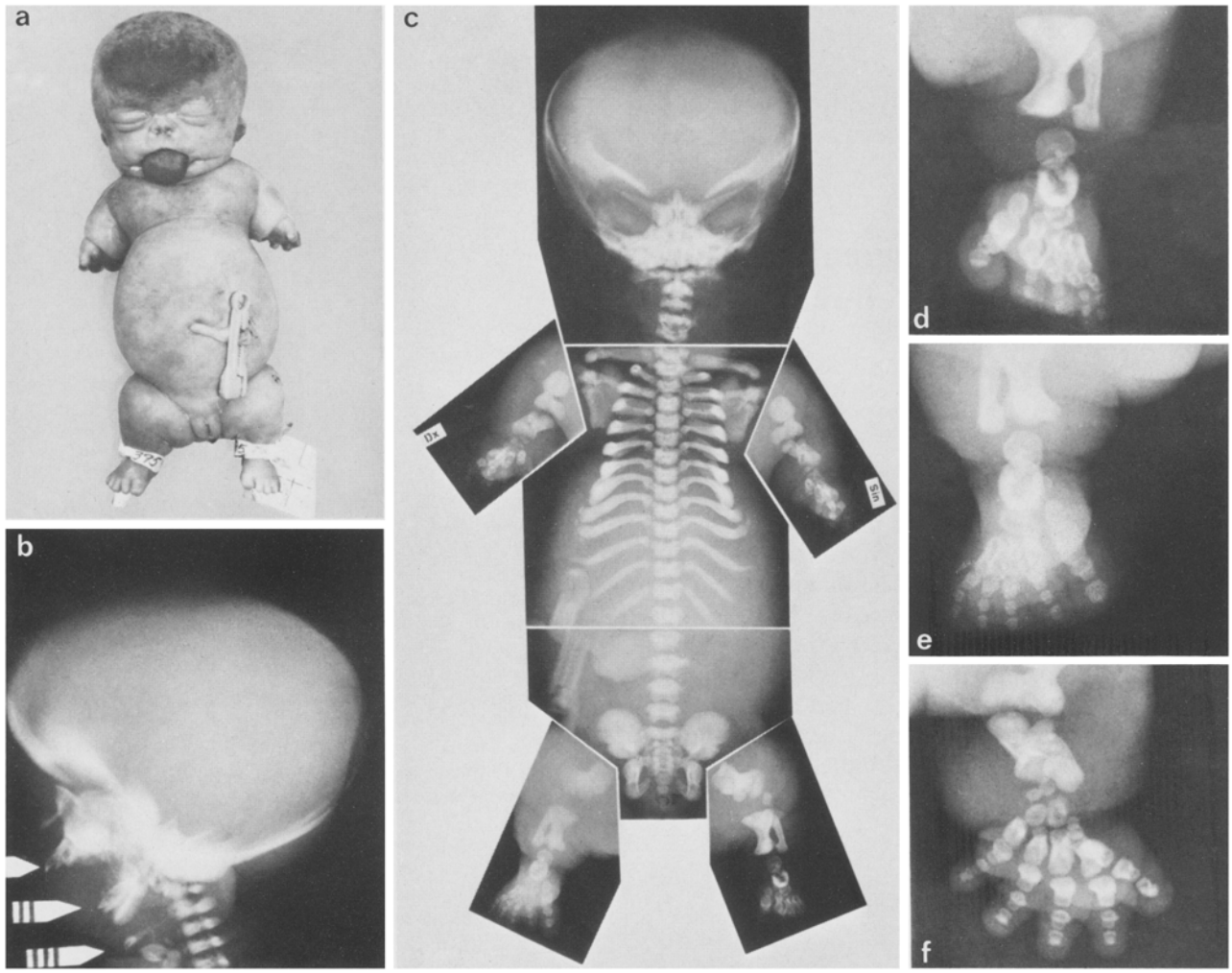

Fig. 1. **a** General appearance. The most notable features are the swollen tongue, the general oedema and the very short limbs. **b** Lateral view of the skull. Marked dysproportion between the neurocranium and the facial skeleton is evident. ⊏⊃ Mineralized incisors protruding forward owing to the large tongue. ⊏⊃ Mandible with two rows of mineralized teeth, decidous and permanent. ⊏⊃ Hyoid bone and ossified laryngeal cartilage. **c** "Babygram" composed of separate films for different parts, all exposed with the same filmfocus distance. **d, e** Details of the feet. Note the markedly advanced ossification. **f** The left wrist and hand – Advanced ossification

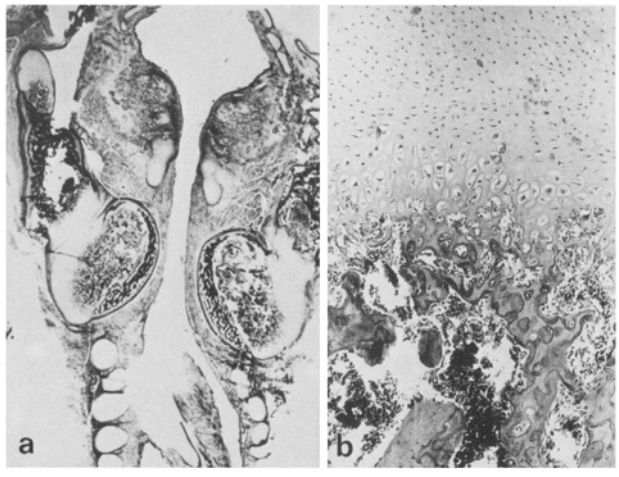

Fig. 2. **a** frontal section through the larynx showing ossification in the thyroid cartilages (H & E; X6). **b** Detail of the epi-metaphyseal junction with irregular bone trabeculae and thin zones of resting and proliferating cartilages (H & E; X 75)

radiological appearance in these diagnoses differ from the present case; achondrogenesis being characterized by a lack of mineralization of the spine and pelvis and thanatophoric dwarfism by flattened vertebral bodies and increased intervertebral spaces combined with certain pathognomonic changes in the pelvic bones and femora.

The most prominent radiologic finding in our case, apart from the deformed and very short extrem-

ities, was the advanced mineralization of the skeleton, with all the phalanges and most carpal and tarsal bones already calcified by the 29th week of gestation. Evidence of accelerated abnormal bone maturation was also found histologically in cartilagenous bones and in the larynx. Such accelerated maturation has been described in diastrophic dwarfism [2], but never to the same extent. Practically all diastrophic dwarfs have shown bilateral club-foot and hand deformities which were not found in our case. Another condition characterized by advanced skeletal maturation is a syndrome described by Marshall et al. [3] and reviewed by Hassan et al. [4]. However, these children were older, had failed to thrive, had dysmorphic faces and were not real dwarfs.

In recent years Kozlowski et al. [5, 6] have published a series of individual cases of "neonatal death dwarfism", all different from each other and from earlier descriptions of dwarfs. We believe that our case may be another example of a hitherto unknown set of skeletal dysplasias which can be added to the growing list of "neonatal death dwarfism". The consanguinity of the parents makes recessive inheritance of the condition probable [7].

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Dr. Ingemar Claësson
Department of Radiology
Children's Hospital
Östra Sjukhuset
S-416 85 Göteborg
Sweden

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